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NEW STEREOSPECIFIC SYNTHESIS OF CHIRAL THIOACETAL MONOSULFOXIDES

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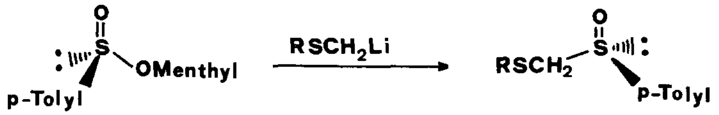
Optically active thioacetal monosulfoxides such as 2 are generally obtained by reaction of α-halogeno-sulfoxides with sodium aryl sulfides.[1a,b] Recent papers[2] on the reactivity of these functionalised sulfoxides prompted us to report a new stereospecific synthesis of chiral thioacetal monosulfoxides.

We have found that the O-menthyl group of an optically active sulfinate ester, (-)-S-1, can be displaced by alkyl- and aryl-thiomethyllithium: this reaction leads to (+)-S thioacetal monosulfoxides 2, 3, 4, with complete inversion of chirality at sulfur atom.



(-)-S-1

(+)-S-2, R = p-Tolyl
(+)-S-3, R = Ph
(+)-S-4, R = Me

A solution of 36 mmol of p-tolyl methyl sulfide and 36 mmol of DABCO in 50 ml of THF at 0°C was treated with 1.61 N n-butyllithium in hexane (24.5 ml). After 15', the resulting mixture, cooled at -78°C, was added with a solution of 18 mmol of (-)-S menthyl p-toluenesulfinate 1 ($|\alpha|^{20}_{D}$ -200°, acetone, c 1) in 60 ml of THF. After 30', at -78°C, the reaction was quenched with saturated NH_4Cl solution. Usual work up and purification by silica gel chromatography (n-hexane - ethyl ether) and crystallization (n-pentane - ethyl ether) lead to 3.5 g of 2 (70% yield). The compound 3 was obtained according to the previous scheme (76% yield) while the compound 4 was obtained using TMEDA instead of DABCO (75% yield), on the basis of the conditions[3] reported for metallation of dimethyl sulfide.

	I.R. ($CHCl_3$)	m.p. (°C)	$\|\alpha\|^{20}_{D}$ (acetone, c 1)	NMR ($CDCl_3$)
2[a]	$\nu_{S=0}$ 1035 cm^{-1}	78-79	+76°[b]	δ=2.32 (3H,s,Me), 2.39 (3H,s,Me), AB system (2H, $\|J_{AB}\|$=13.5 Hz, δ_A4.12, δ_B3.99), 7.00-7.66 (m,8 Arom. H)
3[a]	$\nu_{S=0}$ 1035 cm^{-1}	69-70	+97°	δ=2.39 (3H,s,Me), AB system (2H, $\|J_{AB}\|$=13.4 Hz, δ_A4.16, δ_B4.03), 7.10-7.43 (m,9 Arom. H)
4[a]	$\nu_{S=0}$ 1035 cm^{-1}	44-45	+276°	δ=2.19 (3H,s,Me), 2.42 (3H,s,Me), AB system (2H, $\|J_{AB}\|$=13.5 Hz, δ_A3.74, δ_B3.68), 7.26-7.66 (m,4 Arom. H)

[a] Crystalline samples gave satisfactory elemental analyses

[b] $|\alpha|^{14}_{D}$ +76.8° (acetone, c 0.186) is the reported value for optically pure S-2 (ref. 1b), $|\alpha|^{25}_{D}$ -77° (acetone, c 1) for optically pure R-2 (ref. 1a)

Optical purity: 100% calculated on ^1H NMR spectra in presence of tris[3-(2,2,2-trifluoro-1-hydroxyethylidene)-d-camphorato] europium III as chiral shift reagent. The conditions were pre-established on a racemic sample of 2, obtained from the reaction[4] of CH_2I_2 with $CH_3C_6H_4SNa$ followed by H_2O_2 - CH_3COOH monooxidation.[5] Separate signals are observed for CH_2 groups (2 AB systems, $\Delta\delta$=0.05 ppm) in CCl_4 with a 0.05 molar ratio between the shift reagent and the racemic 2. On the contrary, under the same conditions, only one AB system could be detected, by ^1H NMR of the sample 2 $|\alpha|^{20}_{D}$ +76°, with the chiral shift reagent. The same results were obtained with 3 $|\alpha|^{20}_{D}$ +97° and 4 $|\alpha|^{20}_{D}$ +276°.

The applicability of these compounds in asymmetric nucleophilic acylation is currently under investigation.

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